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Health and Environmental Effects Profile for Merphos

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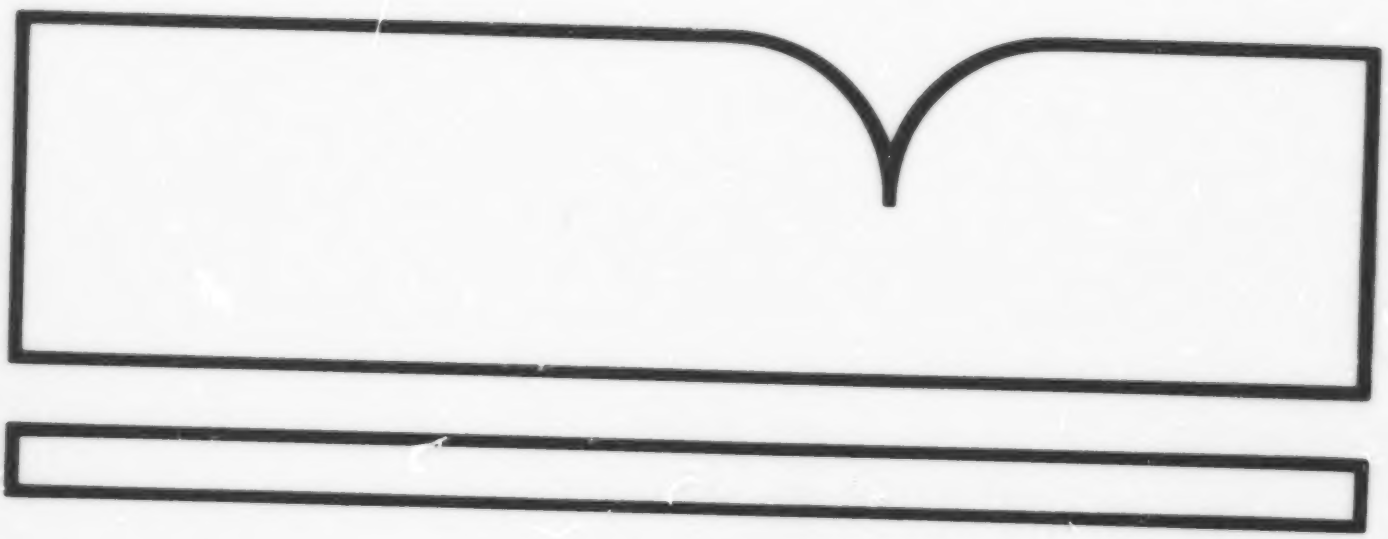

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HEALTH AND ENVIRONMENTAL EFFECTS PROFILE FOR MERPHOS

ENVIRONMENTAL CRITERIA AND ASSESSMENT OFFICE
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16. ABSTRACT

The Health and Environmental Effects Profile for Merphos was prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files were evaluated as they pertained to potential human health, aquatic life and environmental effects of hazardous waste constituents.

Quantitative estimates have been presented provided sufficient data are available. Merphos has been determined to be a systemic toxicant. An Acceptable Daily Intake (ADI), defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect, for Merphos is 1.8×10^{-3} (mg/kg bw/day) for oral exposure.

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PREFACE

Health and Environmental Effects Profiles (HEEPs) are prepared for the Office of Solid Waste by the Office of Health and Environmental Assessment. The HEEPs are intended to support listings of hazardous constituents of a wide range of waste streams under Section 3001 of the Resource Conservation and Recovery Act (RCRA). Both published literature and information obtained from Agency program office files are evaluated as they pertain to potential human health, aquatic life and environmental effects of hazardous waste constituents. The literature searched and the dates of the searches are included in the section titled "Appendix: Literature Searched."

Quantitative estimates are presented provided sufficient data are available. For systemic toxicants, these include, Acceptable Daily Intakes (ADIs) for chronic exposures. An ADI is defined as the amount of a chemical to which humans can be exposed on a daily basis over an extended period of time (usually a lifetime) without suffering a deleterious effect. In the case of suspected carcinogens, ADIs are not estimated in this document series. Instead, a carcinogenic potency factor or q_1^* is provided. These potency estimates are derived for both oral and inhalation exposures where possible. In addition, unit risk estimates for air and drinking water are presented based on inhalation and oral data, respectively.

The first draft of this document was prepared by Syracuse Research Corporation under EPA Contract No. 68-03-3228. The document was subsequently revised after reviews by staff within the Office of Health and Environmental Assessment: Carcinogen Assessment Group, Reproductive Effects Assessment Group, Exposure Assessment Group, and the Environmental Criteria and Assessment Office in Cincinnati.

The HEEPs will become part of the EPA RCRA docket.

ACKNOWLEDGEMENTS

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LIST OF ABBREVIATIONS

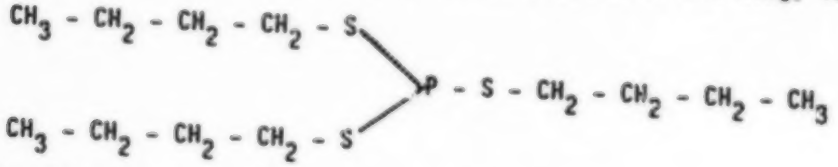
ADI	Acceptable daily intake
i.p.	Intraperitoneal
LD_{50}	Concentration lethal to 50% of recipients
NOEL	No-observed-effect level

1. INTRODUCTION

1.1. STRUCTURE AND CAS NUMBER

Merphos is a synonym for phosphorotrithious acid, S,S,S-tributyl ester. This chemical is also known as phosphorotrithious acid, tributyl ester; S,S,S-tributyl phosphorotrithioite; Deleaf Defoliant; Easy-Off-D; and Folex (NIOSH, 1983). Folex is the trademark for merphos for which U.S. Patent number 2,955,802 was issued to the Mobil Oil Corporation in 1960 (Ouellette and King, 1977).

The structure of merphos is given below (Ouellette and King, 1977):



Molecular Formula: $C_{12}H_{27}PS_3$

Molecular Weight: 298.3

The Chemical Abstracts Service (CAS) Registry number for this compound is 150-50-5.

1.2. PHYSICAL AND CHEMICAL PROPERTIES

Merphos is a pale-yellow liquid with the following properties:

Boiling Point:	115-134°C at 0.08 mm Hg (BCPC, 1977)
Density (d_4^{20}):	0.99-1.01 (BCPC, 1977)
Vapor Pressure:	3.04×10^{-5} mm Hg (Hermann, 1980)
Solubility:	very low solubility in water; very soluble in most organic solvents (BCPC, 1977)
Log K_{ow}:	>5.7 (U.S. EPA, 1981)

1.3. PRODUCTION DATA

Merphos is an herbicide produced by Rhone-Poulenc, Inc., Agrochemical Division, Mount Pleasant, TN (SRI, 1983), and until 1981 was produced by

Mobil Oil Corporation, Mobil Chemical Co., Phosphorus Division, Mount Pleasant, TN (Lawless et al., 1972; USITC, 1981). According to Lawless et al. (1972), the 1971 estimated U.S. pesticide production volume of merphos by Mobil Oil Corp. was 3 million pounds. More recent production data were not available.

Merphos is made by reacting 1-butanethiol and phosphorus trichloride in a solvent (BCPC, 1977).

1.4. USE DATA

Merphos is used as a cotton defoliant at 1.2-2.5 kg/ha (BCPC, 1977).

2. ENVIRONMENTAL FATE AND TRANSPORT PROCESSES

As an herbicide sprayed onto agricultural fields, merphos is likely to enter the atmosphere by wind drift during spray applications, or by volatilization from soil. Its fate in the air is determined by its ready photochemical transformation. Woodrow et al. (1983) reported that during a spray drift test, merphos in the vapor phase underwent atmospheric photooxidation to merphos oxide very rapidly ($t_{1/2}$ ~1 second). By the time the spray drift reached the first sampling site (50 meters from the spray front), oxidation to merphos oxide was essentially complete. Hermann (1980) also reported rapid photooxidation of merphos with a half-life of seconds. When merphos was applied to cotton plants in a laboratory chamber, the major residue detected in the air during the first 2 days after application was 1-butanethiol. Similar results were obtained in field studies, again with high levels of 1-butanethiol detected in the air.

Merphos can enter the aquatic environment through agricultural runoff. The fate of merphos in raw river water was studied by Eichelberger and Lichtenberg (1971). Merphos, added in a concentration of 10 µg/ℓ to Little Miami River water and kept in jars under sunlight and artificial fluorescent lamps underwent 100% chemical oxidation to merphos oxide within 1 hour. Merphos oxide was more persistent, with a $t_{1/2}$ of 1 week.

No information was located regarding the fate and transport of merphos in soil; however, due to its ready degradation in air and water, its persistence in any environmental medium seems unlikely.

3. EXPOSURE

No pertinent monitoring data regarding merphos was located in STORET or any other source. Consulted as part of this project (see Appendix).

4. PHARMACOKINETICS

Pertinent data regarding the absorption, distribution, metabolism or elimination of merphos in mammalian species were not located in the available literature (see Appendix).

5. EFFECTS

5.1. CARCINOGENICITY

Pertinent data regarding the possible carcinogenicity of merphos were not located in the available literature (see Appendix). Merphos is not scheduled for testing by the National Toxicology Program (NTP, 1983).

5.2. MUTAGENICITY

Pertinent data regarding the mutagenicity of merphos were not located in the available literature (see Appendix).

5.3. TERATOGENICITY

Pertinent data regarding the teratogenicity of merphos were not located in the available literature (see Appendix).

5.4. OTHER REPRODUCTIVE EFFECTS

Pertinent data regarding other possible reproductive effects were not located in the available literature (see Appendix).

5.5. CHRONIC AND SUBCHRONIC TOXICITY

In an abstract of a Russian study, Khaitov and Baimuradov (1973) reported that merphos (12 mg/kg/day for an unspecified duration) decreased cholinesterase activity and increased the total protein, sugar, erythrocyte and leukocyte content of rabbit blood. The route of administration was not mentioned.

In describing the general toxic effects of organophosphorous compounds, Norton (1980) indicated that this class of compounds produces delayed neurotoxicity in both chickens and man. Abou-Donia et al. (1980) tested merphos for delayed neurotoxicity in mixed breed hens following topical (to the comb) and oral administration. Topical administration of merphos (20 or 40 mg/kg/day for 90 days) resulted in the production of delayed neurotoxicity in a dose-dependent fashion. In the oral dosing study, 0.1 mg/kg/day in

gelatin capsules for 90 days was the NOEL. Administration of 0.5-40 mg/kg/day resulted in the development of ataxia. A daily dose of 80 mg/kg produced symptoms of late acute toxicity as well as delayed neurotoxicity; symptoms progressed to paralysis followed by death within 12-23 days of the start of treatment.

Graham (1980) developed an *in vitro* model for delayed neurotoxicity using neuroblastoma cell lines. The degree of toxicity of the various organophosphates tested were in the order of merphos $\geq$ DEF $\geq$ EPN > parathion > leptophos $\geq$ TOCP.

5.6. OTHER RELEVANT INFORMATION

A number of authors have determined acute LD_{50} values for merphos in rats and rabbits (Table 5-1). In the rat, toxicity occurs in the order: i.p. > dermal > oral; however, the rabbit seems resistant to the dermal toxicity of merphos.

DuBois and Kinoshita (1968) found that induction of microsomal enzymes by phenobarbital decreased the toxicity of administered merphos i.p. in female rats, but not in male mice.

Abou-Donia et al. (1980) studied acute cholinergic, late acute, and delayed neurotoxic effects in hens following a single oral (100-2000 mg/kg) or topical (1000 mg/kg) application of merphos. The late acute effect occurred 20.-0.25 days after administration and was characterized by a reduced feed consumption and the combs becoming dark and droopy, followed by tremor, paralysis and death. These symptoms were not relieved by atropine sulfate and were presumably produced by a metabolite of merphos, n-butyl mercaptan (1-butanethiol), produced in the gut. Late acute toxicity was not observed following topical administration (1000 mg/kg); however, delayed neurotoxicity was observed in all treated hens.

TABLE 5-1

Acute Toxicity of Merphos

Species	Route	LD_{50} (mg/kg)	Reference
Rat	oral	910	NIOSH, 1983
Rat (male)	oral	1475	Gaines, 1969
Rat (female)	oral	910	Gaines, 1969
Rat (male)	oral	1272	Martin and Worthing, 1977
Rat	dermal	615	NIOSH, 1983
Rat (male)	dermal	690	Gaines, 1969
Rat (female)	dermal	615	Gaines, 1969
Rat	i.p.	76	NIOSH, 1983
Rat (female)	i.p.	124	DuBois and Kinoshita, 1968
Rabbit	dermal	>4600	Martin and Worthing, 1977
Mice (male)	i.p.	68	DuBois and Kinoshita, 1968

i.p. = intraperitoneal

6. AQUATIC TOXICITY

Pertinent data regarding the effects of merphos on aquatic organism were not located in the available literature. Merphos has a very short half-life before being oxidized to merphos oxide and, therefore, does not persist in the environment (Eichelberger and Lichtenberg, 1971).

7. EXISTING GUIDELINES AND STANDARDS

7.1. HUMAN

Existing guidelines or standards for merphos were not located in the available literature.

7.2. AQUATIC

Guidelines and standards for the protection of aquatic organisms from the toxic effects of merphos were not located in the available literature.

.8. RISK ASSESSMENT

Pertinent data regarding the carcinogenicity or mutagenicity of merphos were not located in the available literature as cited in the appendix.

Two subchronic toxicity studies were found. One, a Russian study (Khaitov and Baimuradov, 1973) available as an abstract, reported decreased blood cholinesterase activity in rabbits after administration of 12 mg merphos/kg/day. The duration and route of administration were not specified. In the other study, Abou-Donia et al. (1980) investigated delayed neurotoxic effects in hens treated orally with merphos for 90 days. The NOEL for delayed neurotoxicity in hens was 0.1 mg/kg bw/day; 0.5 mg/kg bw/day produced mild ataxia. No chronic toxicity studies were located in the available literature, and the information from these subchronic studies was considered insufficient for the derivation of an ADI.

Statements concerning available literature in this document refer to published, quotable sources and are in no way meant to imply that confidential data, which this document could not address, are not in existence. These data, which are considered Confidential Business Information (CBI), are available in summary form as a CBI Appendix that can be accessed by individuals with appropriate clearance. Conclusions from the CBI Appendix regarding risk assessment can, however, be presented in this chapter.

Although no studies of chronic duration were available for review in the CBI Appendix, a series of subchronic studies provided a sufficient data base from which to derive an ADI. Based on a NOAEL of 1.8 mg/kg bw/day for decreased plasma and red blood cell cholinesterase activities in rats in a 90-day feeding study and an uncertainty factor of 1000 (a factor of 10 for interspecies extrapolation, a factor of 10 to protect the most sensitive humans and a factor of 10 for the uncertainity associated with extrapolating for a subchronic NOAEL), an ADI of 0.0018 mg/kg bw/day or 0.126 mg/day for a 70 kg man is recommended.

9. REFERENCES

Abou-Donia, M.B., D.O Graham, P.R. Timmons and B.L. Reichert. 1980. Late acute, delayed neurotoxic and cholinergic effects of S,S,S-tributyl phosphorotrithioite (merphos) in hens. Toxicol. Appl. Pharmacol. 53(3): 439-457.

BCPC (British Crop Protection Council). 1977. Pesticide Manual, 5th ed., H. Martin, and C.R. Worthing, Ed. p. 521.

DuBois, K.P. and F.K. Kinoshita. 1968. Influence of induction of hepatic microsomal enzymes by phenobarbital on toxicity of organic phosphate insecticides. Proc. Soc. Exp. Biol. Med. 129(3): 699-702.

Eichelberger, J.W. and J.J. Lichtenberg. 1971. Persistence of pesticides in river water. Environ. Sci. Technol. 5(6): 541-544.

Gaines, T.B. 1969. Acute toxicity of pesticides. Toxicol. Appl. Pharmacol. 14(3): 515-534.

Graham, D.G. 1980. Development of an <u>in vitro</u> model for screening organophosphates for neurotoxicity. Report: ISS EPA 600/1-80-016; Order No. PB80-169428. p. 43.

Hermann, B.W. 1980. Atmosphere residues of the defoliants Def., Folex, and their sulfur-containing byproducts near treated cotton fields. Diss. Abstr. Int. B 1981. 41(11): 4104.

Khaitov, R.Kh. and T.B. Baimuradov. 1973. Pathogenesis of rabbit poisoning with Folex. Tr. Uzb. Nauchno-Issled. Vet. Inst. 23: 187. (Chem. Abstr. 83: 202543d)

Lawless, E.W., R. von Rumker and T.L. Ferguson. 1972. The Pollution Potential in Pesticide Manufacturing. Prepared for U.S. EPA by Midwest Research Institute under Contract No. 69-01-0142. U.S. EPA, Office of Water Programs. Tech. Studies Report. TS-00-72-04.

Martin, H. and C.R. Worthing, Ed. 1977. Pesticide Manual. Basic information on the chemicals used as active components of pesticides. British Crop Protection Council, Worcestershire, England.

NIOSH (National Institute for Occupational Safety and Health). 1983. RTECS (Register of Toxic Effects of Chemical Substances). May, 1983: Online.

Norton, S. 1980. Toxic response of the central nervous system. In: Casarett and Doull's Toxicology. The Basic Science of Poisons, J. Doull, C.D. Klaassen and M.O. Amdur, Ed. Macmillan Publishing Co., Inc. p. 195-196.

NTP (National Toxicology Program). 1983. Chemicals on Standard Protocol: Management Status Report, April 20, 1983.

Ouellette, R.P. and J.A. King. 1977. Chemical Week Pesticides Register. McGraw-Hill Book Company, NY. p. 198.

SRI (Stanford Research Institute International). 1983. Directory of Chemical Producers. SRI International, Menlo Park, CA.

U.S. EPA. 1981. Acetate, aldicarb, carbophenothion, DEF, EPN, ethoprop, methyl parathion, and pharate: Their acute and chronic toxicity, bioconcentration potential, and persistence as related to marine environments. Prepared for the Office of Pesticides and Toxic Substances by Environmental Research Laboratory, Gulf Breeze, FL. EPA 600/4-81-041. PB 81-244477. 275 p.

USITC (United States International Trade Commission). 1981. Synthetic Organic Chemicals, United States Production and Sales, 1981. USITC Publ. 1292. USITC, Washington, DC.

Woodrow, J.E., D.B. Crosby and J.N. Seiber. 1983. Vapor phase photochemistry of pesticides. Residue Rev. 85: 111-125.

APPENDIX:

LITERATURE SEARCHED

This profile is based on data identified by computerized literature searches of the following:

CA SEARCH (Files 308, 309, 310, 311, 320)
TOXLINE
MEDLINE
RTECS
SCI SEARCH
OHM TADS
STORET
SRC Environmental Fate Data Bases
SANSS
AQUIRE

These searches were conducted in May, 1983. In addition, hand searches were made of Chemical Abstracts (Collective Indices 7 and 8th), and the following secondary sources were reviewed:

ACGIH (American Conference of Governmental Industrial Hygienists). 1980. TLVs: Documentation of the Threshold Limit Values, 4th ed. (Includes Supplemental Documentation, 1981). Cincinnati, OH. p. 486.

ACGIH (American Conference of Governmental Industrial Hygienists). 1982. TLVs: Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment. Cincinnati, OH. p. 94.

BCPC (British Crop Protection Council). 1977. Pesticide Manual, 5th ed. H. Martin and C.R. Worthing, Ed. British Crop Protection Council. p. 593.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2A. John Wiley and Sons, NY. p. 2878.

Clayton, G.D. and F.E. Clayton, Ed. 1981. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2B. John Wiley and Sons, NY. p. 2879-3816.

Clayton, G.D. and F.E. Clayton, Ed. 1982. Patty's Industrial Hygiene and Toxicology, 3rd rev. ed., Vol. 2C. John Wiley and Sons, NY. p. 3817-5112.

Grayson, M. and D. Eckroth, Ed. 1978-1983. Kirk-Othmer Encyclopedia of Chemical Technology, 3rd ed. John Wiley and Sons, NY. 23 Volumes.

Hamilton, A. and H.L. Hardy. 1974. Industrial Toxicology. 3rd ed. Publishing Sciences Group, Inc., MA. p. 575.

ITII (International Technical Information Institute). 1982. Toxic and Hazardous Industrial Chemicals Safety Manual for Handling and Disposal with Toxicity and Hazard Data. ITII, Tokyo, Japan. p. 700.

NTP (National Toxicology Program). 1983. Carcinogenesis Testing Program. Chemicals on Standard Protocol. Management Status.

Ouellette, R.P. and J.A. King. 1977. Chemical Week Pesticide Register. McGraw-Hill Book Co., NY.

Sax, I.N. 1979. Dangerous Properties of Industrial Materials. 5th ed. Van Nostrand Reinhold Co., NY.

SRI (Stanford Research Institute). 1983. Directory of Chemical Producers. Stanford, CA.

U.S. EPA. 1982. Chemical Activities Status Report. 3rd ed. (EPACASR). Offices of Pesticides and Toxic Substances, Washington, DC. EPA 560/TIIS-82-002b.

U.S. EPA. 1982. Status Report on Rebuttable Presumption Against Registration (RPAR) or Special Review Process. Registration Standards and the Data Call In Program. Office of Pesticide Programs, Washington, DC.

U.S. EPA. 1983. CHIB Existing Chemical Assessment Tracking System. Name and CAS Number Ordered Indexes. Office of Toxic Substances, Washington, DC.

USITC (United States International Trade Commission). 1982. Synthetic Organic Chemicals. U.S. Production and Sales, 1981. Washington, DC.

Verschueren, K. 1983. Handbook of Environmental Data on Organic Chemicals, 2nd ed. Van Nostrand Reinhold Co., NY.